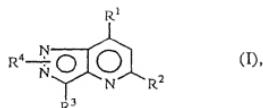


Claims

1. Use of compounds of formula (I)



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including the stereoisomers and the pharmaceutically acceptable acid addition salt forms thereof, wherein

R¹ is C₁-6alkyl, NR⁵R⁶, OR⁶ or SR⁶;

R² is C₁-6alkyl, C₁-6alkyloxy, or C₁-6alkylthio;

10 R³ is Ar¹ or Het¹;

R⁴ is hydrogen or C₁-6alkyl;

R⁵ is hydrogen, C₁-8alkyl, mono- or di(C₃-6cycloalkyl)methyl, C₃-6cycloalkyl, C₃-6alkenyl, hydroxyC₁-6alkyl, C₁-6alkylcarbonyloxyC₁-6alkyl, mono- or di(C₁-6alkyl)aminoC₁-6alkyl or C₁-6alkyloxyC₁-6alkyl;

15 R⁶ is C₁-8alkyl, mono- or di(C₃-6cycloalkyl)methyl, Ar²C₁-6alkyl, Ar²oxyC₁-6alkyl, C₁-6alkyloxyC₁-6alkyl, hydroxyC₁-6alkyl, C₃-6alkenyl, thiienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C₁-6alkylthioC₁-6alkyl, mono- or di(C₁-6alkyl)aminoC₁-6alkyl, di(C₁-6alkyl)amino, or C₁-6alkylcarbonylC₁-6alkyl;

20 or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, homopiperidinyl, morpholinyl, or thiomorpholinyl group, optionally substituted with 1 or 2 substituents each independently selected from C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl;

25 Ar¹ is phenyl; naphtyl; or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-6alkyl, trifluoromethyl, hydroxy, cyano, C₁-6alkyloxy, benzyl, benzyloxy, C₁-6alkylthio, nitro, amino and mono- or di(C₁-6alkyl)amino;

30 Het¹ is pyridinyl; pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, C₁-6alkyl, trifluoromethyl, hydroxy, cyano, C₁-6alkyloxy, benzyloxy, C₁-6alkylthio, nitro, amino, and mono- or di(C₁-6alkyl)amino; and

Ar² is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C₁-6alkyl, C₁-6alkyloxy, di(C₁-6alkyl)aminoC₁-6alkyl, or trifluoromethyl; or pyridinyl; for the manufacture of a medicament for treating physiological conditions or disorders arising from the hypersecretion of corticotropin-releasing factor (CRF).

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2. Use of a compound according to claim 1 wherein R¹ is NR⁵R⁶ wherein R⁵ is hydrogen or C₁-6alkyl; and R⁶ is C₁-6alkyl or C₃-6cycloalkylmethyl; or R¹ is OR⁶ or SR⁶ wherein R⁶ is C₁-6alkyl; R² is C₁-6alkyl; R³ is a phenyl substituted with 1, 2 or 3 substituents each independently selected from C₁-6alkyl, C₁-6alkyloxy or halo; or R³ is a pyridinyl substituted with 1, 2 or 3 substituents each independently selected from halo, amino, nitro, trifluoromethyl, mono- or di(C₁-6alkyl)amino, or C₁-6alkyl; and R⁴ is hydrogen or C₁-6alkyl.

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15 3. A compound of formula (I-1) wherein R¹ to R⁴ are defined as in claim 1 and wherein at least R¹ is C₁-6alkyl; OR⁶; SR⁶; or NR⁵R⁶ wherein R⁵ is mono- or di(C₃-6cycloalkyl)methyl, C₃-6cycloalkyl, C₃-6alkenyl, hydroxyC₁-6alkyl, C₁-6alkylcarbonyloxyC₁-6alkyl, mono- or di(C₁-6alkyl)aminoC₁-6alkyl or C₁-6alkyloxyC₁-6alkyl, and R⁶ is mono- or di(C₃-6cycloalkyl)methyl, Ar²C₁-6alkyl, Ar²oxyC₁-6alkyl, hydroxyC₁-6alkyl, C₁-6alkyloxyC₁-6alkyl, C₃-6alkenyl, thiienylmethyl, furanylmethyl, tetrahydrofuranylmethyl, C₁-6alkylthioC₁-6alkyl, C₁-6alkylcarbonylC₁-6alkyl, mono- or di(C₁-6alkyl)aminoC₁-6alkyl, or di(C₁-6alkyl)amino; or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl; or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl; or

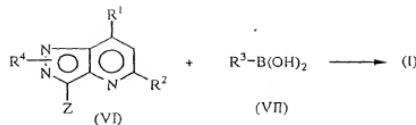
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25 at least R³ is Het¹ or Ar¹ wherein Ar¹ is naphthyl; or phenyl substituted with 3 substituents each independently selected from halo, C₁-6alkyl, trifluoromethyl, hydroxy, cyano, C₁-6alkyloxy, benzyl, benzyloxy, C₁-6alkylthio, nitro, amino and mono- or di(C₁-6alkyl)amino.

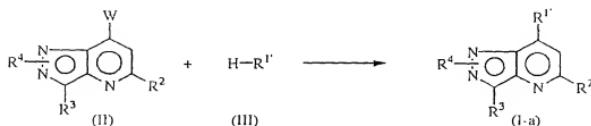
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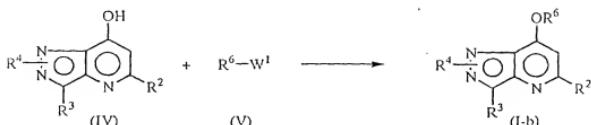
4. A compound according to claim 3 wherein R¹ is a radical of formula NR⁵R⁶ wherein R⁵ is mono- or di(C₃-6cycloalkyl)-methyl, C₃-6cycloalkyl, C₃-6alkenyl, hydroxyC₁-6alkyl, C₁-6alkylcarbonyloxyC₁-6alkyl, mono- or di(C₁-6alkyl)amino-C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl, and R⁶ is mono- or di(C₃-6cycloalkyl)methyl, Ar²C₁-6alkyl, Ar²oxyC₁-6alkyl, hydroxyC₁-6alkyl, C₁-6alkyloxyC₁-6alkyl, C₃-6alkenyl, thiethylmethyl, furanyl methyl, tetrahydrofuranyl methyl, C₁-6alkylthioC₁-6alkyl, C₁-6alkylcarbonylC₁-6alkyl, mono- or di(C₁-6alkyl)aminoC₁-6alkyl, or di(C₁-6alkyl)amino.
- 10 5. A compound according to claim 3 wherein R¹ is a radical of formula NR⁵R⁶ wherein R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a pyrrolidinyl, piperidinyl, or homopiperidinyl, each substituted with 1 or 2 substituents independently selected from C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl; or R⁵ and R⁶ taken together with the nitrogen atom to which they are attached may form a morpholinyl or a thiomorpholinyl group, optionally substituted with 1 or 2 substituents independently selected from C₁-6alkyl or C₁-6alkyloxyC₁-6alkyl.
- 20 6. A compound according to claim 3 wherein R³ is Het¹ or Ar¹ wherein Ar¹ is naphtyl; or phenyl substituted with 3 substituents each independently selected from halo, C₁-6alkyl, trifluoromethyl, hydroxy, cyano, C₁-6alkyloxy, benzyl, benzyloxy, C₁-6alkylthio, nitro, amino or mono- or di(C₁-6alkyl)amino.
- 25 7. A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6.
- 30 8. A process for preparing a composition as claimed in claim 7 wherein a therapeutically effective amount of a compound as claimed in any one of claims 3 to 6 is intimately mixed with a pharmaceutically acceptable carrier.
9. A compound according to any one of claims 3 to 6 for use as a medicine.
- 35 10. A process of preparing a compound of formula (I-1) as claimed in claim 3 wherein a) intermediates of formula (VI) are reacted with intermediates of formula (VII) under Suzuki coupling conditions;



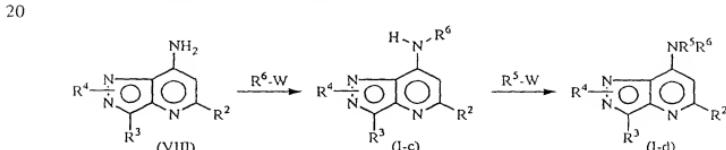
5 b) an intermediate of formula (II) is reacted with an intermediate of formula (III),
 wherein $\text{R}^{1'}$ has the meaning of R^1 other than $\text{C}_1\text{-alkyl}$, thereby yielding
 compounds of formula (I-a);



10 c) an intermediate of formula (IV) is *O*-alkylated with an intermediate of formula
 (V) in a reaction-inert solvent and in the presence of a suitable base, yielding
 compounds of formula (I-b), defined as compounds of formula (I) wherein R^1 is
 OR^6 ,



15 d) an intermediate of formula (VII) is *N*-alkylated with an intermediate of formula
 R^6-W in a reaction-inert solvent and in the presence of a suitable base, yielding
 compounds of formula (I-c), which can be further *N*-alkylated with an
 intermediate of formula R^5-W



wherein in the above reaction schemes the radicals R¹ to R⁶, are as defined in claim 1, Z is bromo or iodo and W and W¹ are appropriate leaving groups;

5 or, if desired, compounds of formula (I) are converted into each other following art-known transformation reactions; and further, if desired, compounds of formula (I) are converted into an acid addition salt by treatment with an acid, or conversely, the acid addition salt forms are converted into the free base by treatment with alkali; and, if desired, preparing stereochemically isomeric forms thereof.